Claims

1. A method to separate cells according to a product secreted and released by the cells wherein the separation of cells is effected according to the degree to which they are labeled with the product, the method comprising the steps of:

coupling the surface of the cells to a capture moiety and culturing the cells under conditions wherein the product is secreted, released and specifically bound to the capture moiety; and

separating the cells on the basis of the bound product.

2. The method according to claim 1 further comprising the step of labeling the product prior to separation.

3. The method according to claim 2 wherein the product is labeled with a label moiety.

4. The method according to claim 3 wherein the label moiety is an antibody specific for the product.

5. The method according to claim 1 wherein the label moiety is fluorochromated and the separation is conducted by cell sorting.

6. The method according to claim 1 wherein the label moiety is magnetizable and the separation is conducted in a magnetic field of sufficient strength to magnetized the label moiety.

7. The method according to claim 6 wherein the label moiety comprises colloidal magnetic particles with a typical diameter of about 5 to 200 nm.

8. The method according to claim 1 wherein the capture moiety is an antibody or an antigen-binding fragment thereof.

9. The method according to claim 8 wherein the antibody or antigen binding fragment thereof is bispecific.

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10. The method according to claim 1 wherein the coupling is through a lipid anchor attached to the capture moiety optionally through a linking moiety.

11. The method according to claim 1 wherein the coupling is through an antibody or an antigen-binding fragment thereof attached to the capture moiety, optionally through a linker.

12. The method according to claim 1 wherein the coupling is through direct chemical coupling of the capture moiety to components on the cell surface, optionally through a linker.

13. The method according to claim 9 wherein the coupling is through specific binding of the antibody to the cell.

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14. A method to label cells with a product secreted and released by the cells, which method comprises:

coupling the surface of the cells to a capture moiety;

culturing the cells under conditions wherein the product is secreted and released, wherein the product is captured by the capture moiety.

15. The method according to claim 14 wherein the product is labeled with label moiety.

16. The method according to claim 15 wherein the label moiety is an antibody.

17. The method according to claim 14 wherein the specific binding partner is an antibody or an antigen-binding fragment thereof.

18. The method according to claim 17 wherein the antibody is bispecific.

19. The method according to claim 14 wherein the coupling is through a lipid anchor attached to the specific binding partner optionally through a linking moiety.

20. The method according to claim 14 wherein the coupling is through an antibody or an antigen-binding fragment thereof attached to the specific binding partner optionally through a linker.

21. The method according to claim 18 wherein the coupling is through specific binding of the antibody to the cell.

22. A composition of matter which comprises cells capable of capturing a product secreted and released by the cells wherein the surface of the cells is

coupled to a capture moiety, and wherein the specific binding partner is not a hapten.

23. The composition according to claim 22 which is further coupled to the product.

24. The composition according to claim 22 wherein the capture moiety is an antibody or an antigen-binding fragment thereof.

25. The composition according to claim 24 wherein the antibody is bispecific.

26. The composition according to claim 22 wherein the coupling is through a lipid anchor attached to the capture moiety optionally through a linking moiety.

27. The composition according to claim 22 wherein the coupling is through an antibody or an antigen-binding fragment thereof attached to the capture moiety, optionally through a linker.

28. The composition according to claim 25 wherein the coupling is through specific binding of the antibody to the cell.

29. Cells and progeny thereof separated according to the method of claim 1.

30. Cells separated according to the method of claim 1.

31. A method of analyzing a population of cells to identify or enumerate the cells that secrete an

amount of product relative to other cells in the population, the method comprising the steps of:

labeling the cells by the method according to claim 14,

labeling the cells with at least one additional label that does not label the captured product, and

detecting the amount of product label relative to the additional label.

32. A method of determining a distribution of secretory activity in a population of cells, the method comprising the steps of:

labeling cells by the method according to claim 14, and

determining the amount of product label per cell.

33. The method according to claim 14 further comprising the steps of:

determining the amount and type of product label per cell wherein distribution of secreted product type and secretory activity for each secreted product type in a population of cells is determined.

34. A kit for use in the detection of cells that secrete a desired product, the kit comprising:

a product capture system comprised of at least one anchor moiety and at least one capture moiety; and

at least one label moiety.

35. A kit for use in the detection of cells that secrete a desired product, the kit comprising:

at least one bispecific antibody having at least one antigen recognition site for at least one cell

type and at least one antigen recognition site specific for the product, and

at least one label moiety.

36. The kit according to claim 35 wherein the at least one bispecific antibody and the at least one label moiety are in a single vial.

37. The kit according to claim 35 wherein the at least one bispecific antibody binds to the cell through a cell surface molecule.

38. The kit according to claim 37 wherein the cell surface molecule is a naturally occurring cell surface protein.

39. The kit according to claim 37 wherein the cell surface molecule is a cell surface marker.

40. The kit according to claim 39 wherein the cell surface molecule is selected from the group consisting of CD4, CD8, CD19, CD20, CD14, CD16, CD15, CD45, Class I MHC molecules and Class II molecules, CD34, CD38, CD33, CD56, T cell receptor, Fc receptor, β_2-microglobulin, and immunoglobulin.

41. The kit according to claim 34 wherein the incubation conditions include a high viscosity or gel forming medium.

42. The kit according to claim 41 wherein the medium is selected from the group consisting of gelatin, agarose, alginate and combination thereof.

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43. The kit according to claim 37 wherein the label moiety is an antibody.

44. The kit according to claim 43 wherein the antibody comprises a detectable label.

45. The kit according to claim 44 wherein the detectable label is selected from the group consisting of fluorophores, radioactive isotopes, chromophores, and magnetic particles.

46. The kit according to claim 45 wherein the label moiety is detected by fluorescence activated cell sorting.

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47. The kit according to claim 37 wherein the label moiety is detected by a third antibody.

48. The kit according to claim 47 wherein the label moiety is coupled to digoxigenin and the third antibody is specific for digoxigenin.

49. The kit according to claim 47 wherein the third antibody comprises a detectable label.

50. The kit according to claim 35 further comprising a biological modifier.

51. The kit according to claim 35 further comprising a cell-cell cross-contamination reducing capture system.

52. A method for identifying cells secreting product comprising the steps of:

combining a mixed population of cells with at least one first, bispecific, antibody, each antibody, having combining sites specific for a cell surface molecule and at least one product;

incubating the combination under conditions and for a time sufficient to allow the cells to secrete the at least one product;

adding at least one label moiety; and

detecting the at least one label moiety.

53. The method according to claim 52 further comprising the step of separating the cells secreting the product from the mixed cell population.

54. The method according to claim 53 wherein the cell surface molecule is a naturally occurring cell surface protein.

55. The method according to claim 54 wherein the protein is a cell surface marker.

56. The method according to claim 55 wherein the cell surface marker is selected from the group consisting of CD4, CD8, CD19, CD20, CD14, CD16, CD15, CD45, Class I MHC molecules and Class II MHC molecules, CD34, CD38, CD33, CD56, T cell receptor, Fc receptor, β_2-microglobulin, and immunoglobulin.

57. The method according to claim 52 wherein the incubation conditions include a high viscosity or gel forming medium.

58. The method according to claim 52 wherein the label moiety is an antibody.

59. The method according to claim 58 wherein the antibody comprises a detectable label.

60. The method according to claim 59 wherein the label is selected from the group consisting of fluorophores, radioactive isotopes, chromophores, and magnetic particles.

61. The method according to claim 60 wherein the label moiety is detected by fluorescence activated cell sorting.

62. The method according to claim 61 wherein the label moiety is detected by a third antibody.

63. The method according to claim 62 wherein the label moiety is coupled to digoxigenin and the third antibody is specific for digoxigenin.

64. The method according to claim 62 wherein the third antibody comprises a detectable label.

65. The method according to claim 64 wherein the label is selected from the group consisting of fluorophores, radioactive isotopes, chromophores, and magnetic particles.

66. The method according to claim 65 wherein the label moiety is detected by fluorescence activated cell sorting.

67. The method according to claim 52 wherein the label moiety comprises a magnetizable moiety.